

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
15 July 2004 (15.07.2004)

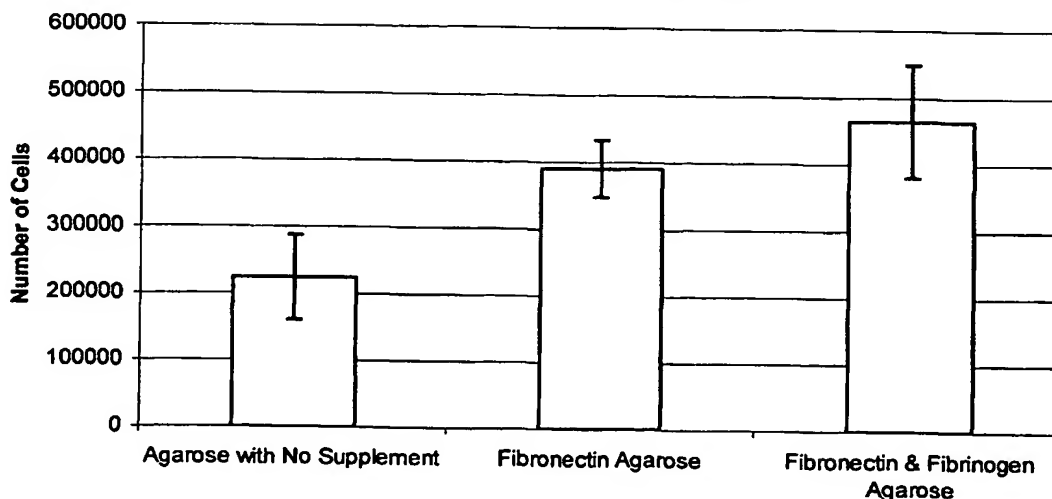
PCT

(10) International Publication Number  
**WO 2004/058305 A3**

- (51) International Patent Classification<sup>7</sup>: **C12N 11/04**, A61K 35/00
- (21) International Application Number: PCT/CA2003/002008
- (22) International Filing Date: 24 December 2003 (24.12.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/435,858 24 December 2002 (24.12.2002) US
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report: 31 March 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ENCAPSULATED CELL FOR THERAPY

Number of Cells Coming Out



(57) Abstract: Cell therapy comprises encapsulating a cell with an integrin or other cell interaction factor, for administration to a mammal. The cells may express a therapeutic transgene or the cells may be regenerative.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/CA 03/02008

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N11/04 A61K35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RAMDI HAFIDA ET AL: "Influence of matricial molecules on growth and differentiation of entrapped chondrocytes" EXPERIMENTAL CELL RESEARCH, vol. 207, no. 2, 1993, pages 449-454, XP002275507 ISSN: 0014-4827 page 449, left-hand column, paragraph 1 - right-hand column, paragraph 1 page 450, left-hand column, paragraphs 1,2 page 451, right-hand column, paragraph 2 page 452, left-hand column, paragraph 2 page 453, right-hand column - page 454, paragraph 4</p> <p>----- -/-</p>	<p>1,2, 10-37</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 March 2004

Date of mailing of the international search report

07. 09. 2004

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/02008

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE BIOSIS [Online]  BIOSCIENCES INFORMATION SERVICE,  PHILADELPHIA, PA, US; 1995,  JAIN KANTI ET AL: "Retrievable,  replaceable, macroencapsulated pancreatic  islet xenografts"  XP002275511  Database accession no. PREV199598235605  abstract  &amp; TRANSPLANTATION (BALTIMORE),  vol. 59, no. 3, 1995, pages 319-324,  ISSN: 0041-1337</p>	1,2, 10-37
X	<p>-----  WO 98/05304 A (LI REBECCA  ;CYTOTHERAPEUTICS INC (US); HAZLETT TYRONE  F (US)) 12 February 1998 (1998-02-12)  page 3, line 17 - page 4, line 29  page 8, line 9 - page 9, line 23</p>	1,2, 10-37
X	<p>-----  WO 95/19430 A (JAIN KANTI ;ROGOSIN INST  (US); RUBIN ALBERT L (US))  20 July 1995 (1995-07-20)  page 5, line 1 - line 27  page 10, line 26 - page 11, line 19  page 15, line 15 - line 24</p>	1,2, 10-37
A	<p>-----  DATABASE MEDLINE [Online]  US NATIONAL LIBRARY OF MEDICINE (NLM),  BETHESDA, MD, US;  MARLER ET AL: "Soft-tissue augmentation  with injectable alginate and syngeneic  fibroblasts"  XP002275512  Database accession no. NLM10839402  abstract  &amp; PLASTIC AND RECONSTRUCTIVE SURGERY,  vol. 105, 2000, pages 2049-2058,</p>	
A	<p>-----  DATABASE MEDLINE [Online]  US NATIONAL LIBRARY OF MEDICINE (NLM),  BETHESDA, MD, US;  HALBERSTADT ET AL: "A hydrogel material  for plastic and reconstructive  applications injected into the  subcutaneous space of a sheep"  XP002275513  Database accession no. NLM12031119  abstract  &amp; TISSUE ENGINEERING,  vol. 8, April 2002 (2002-04), pages  309-319,</p> <p>-----  -/--</p>	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/02008

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE BIOSIS [Online]  BIOSCIENCES INFORMATION SERVICE,  PHILADELPHIA, PA, US; July 2002 (2002-07),  PARK KEUN-HONG: "Improved long-term  culture of hepatocytes in a hydrogel  containing Arg-Gly-Asp (RGD)"  XP002275514  Database accession no. PREV200200500968  abstract  &amp; BIOTECHNOLOGY LETTERS,  vol. 24, no. 14, July 2002 (2002-07),  pages 1131-1135,  ISSN: 0141-5492</p> <p>-----</p>	
A	<p>BURDICK JASON A ET AL:  "Photoencapsulation of osteoblasts in  injectable RGD-modified PEG hydrogels for  bone tissue engineering"  BIOMATERIALS,  vol. 23, no. 22, November 2002 (2002-11),  pages 4315-4323, XP002275508  ISSN: 0142-9612  page 4316, left-hand column, paragraph 5 -  right-hand column, paragraph 1  page 4321, right-hand column, paragraphs  1,2  page 4322, left-hand column, paragraph 2</p> <p>-----</p>	
A	<p>NUTTELMAN CHARLES R ET AL: "Attachment of  fibronectin to poly(vinyl alcohol)  hydrogels promotes NIH3T3 cell adhesion,  proliferation, and migration"  JOURNAL OF BIOMEDICAL MATERIALS RESEARCH,  vol. 57, no. 2, November 2001 (2001-11),  pages 217-223, XP002275509  ISSN: 0021-9304  page 217  abstract</p> <p>-----</p>	
A	<p>MANN BRENDA K ET AL: "Smooth muscle cell  growth in photopolymerized hydrogels with  cell adhesive and proteolytically  degradable domains: Synthetic ECM analogs  for tissue engineering"  BIOMATERIALS,  vol. 22, no. 22, November 2001 (2001-11),  pages 3045-3051, XP002275510  ISSN: 0142-9612  page 3045  abstract  page 3047, right-hand column, paragraph 2</p> <p>-----</p> <p>-/--</p>	

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/02008

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE BIOSIS [Online]  BIOSCIENCES INFORMATION SERVICE,  PHILADELPHIA, PA, US;  January 1999 (1999-01),  ROWLEY JON A ET AL: "Alginate hydrogels as  synthetic extracellular matrix materials"  XP002275515  Database accession no. PREV199900058021  abstract  &amp; BIOMATERIALS,  vol. 20, no. 1, January 1999 (1999-01),  pages 45-53,  ISSN: 0142-9612</p>	
P,A	<p>-----  DATABASE MEDLINE [Online]  US NATIONAL LIBRARY OF MEDICINE (NLM),  BETHESDA, MD, US;  KOH ET AL: "Molding of hydrogel  microstructures to create multiphenotype  cell microarrays"  XP002275516  Database accession no. NLM14588018  abstract  &amp; ANALYTICAL CHEMISTRY,  vol. 75, 1 November 2003 (2003-11-01),  pages 5783-5789,</p>	
P,A	<p>-----  KAROUBI GOLNAZ ET AL: "Cell  micro-encapsulation with integrin binding  proteins prevents anoikis: Implications  for adherent cell therapy."  CIRCULATION,  vol. 108, no. 17 Supplement,  28 October 2003 (2003-10-28), pages  IV-286, XP008029277  American Heart Association Scientific  Sessions 2003;Orlando, FL, USA; November  09-12, 2003  ISSN: 0009-7322 (ISSN print)  abstract  -----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CA 03/02008

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 24, 25, 28, 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Partially 1, 2, 10-37

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 24, 25, 28, 29 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: Partially 1, 2, 10-37

A method of encapsulating a cell, wherein the method used results in the encapsulation product including an 'integrin binding partner', and wherein said 'integrin binding partner' is a collagen; use of products obtainable thereby, kit for use therein

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2. claims: Partially 1, 2, 10-37; completely 3-5, 9

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of fibronectin, vitronectin, von Willebrand Factor, tenascin, laminin, fibrinogen, thrombospondin, an RGD [1 letter amino acid code used] containing peptide, fibrin, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

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3. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is a peptide containing the sequence LDV [1 letter amino acid code used], and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

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4. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is a peptide containing the sequence HHLGGAKQAGDV [1 letter amino acid code used], and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

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5. claims: Partially 1, 2, 10-37

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of VCAM-1, MAdCAM-1, LFA-1, Mac-1, ICAM-1, ICAM-2, ICAM-3, complement component C3bi, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

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6. claims: Partially 1, 2, 10-37; completely 6-8



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

As 1, but wherein the 'integrin binding partner' is selected from the group consisting of Factor X, FXIII, FXIIIa, and insofar as the subject matter of the invention does not relate to any in any of the other inventions listed herein

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 03/02008

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9805304	A	12-02-1998	US 6054142 A	25-04-2000
			AT 250435 T	15-10-2003
			AU 723826 B2	07-09-2000
			AU 3823697 A	25-02-1998
			CA 2258483 A1	12-02-1998
			DE 69725149 D1	30-10-2003
			DE 69725149 T2	03-06-2004
			DK 918509 T3	26-01-2004
			EP 0918509 A1	02-06-1999
			ES 2208938 T3	16-06-2004
			JP 2000515551 T	21-11-2000
			WO 9805304 A1	12-02-1998
			US 6231879 B1	15-05-2001
-----				
WO 9519430	A	20-07-1995	AU 681240 B2	21-08-1997
			AU 1526795 A	01-08-1995
			CA 2181156 A1	20-07-1995
			CN 1141650 A ,B	29-01-1997
			EP 1418228 A1	12-05-2004
			EP 0742818 A1	20-11-1996
			FI 962841 A	12-09-1996
			IL 112330 A	26-01-1999
			JP 9510868 T	04-11-1997
			NO 962955 A	11-09-1996
			NZ 278809 A	25-03-1998
			NZ 329619 A	29-09-1999
			RU 2177503 C2	27-12-2001
			RU 2208636 C2	20-07-2003
			WO 9519430 A1	20-07-1995
			US RE38027 E1	11-03-2003
			US 5643569 A	01-07-1997
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